

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
22 January 2004 (22.01.2004)

PCT

(10) International Publication Number
WO 2004/007512 A2

- (51) International Patent Classification⁷: C07H 07065-0907 (US). PRAKASH, Thazha, P. [IN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US).
- (21) International Application Number: PCT/US2003/021589 (74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).
- (22) International Filing Date: 11 July 2003 (11.07.2003) (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/396,252 16 July 2002 (16.07.2002) US
- (71) Applicants (*for all designated States except US*): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). ISIS PHARMACEUTICALS, INC. [US/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): BHAT, Balkrishen [IN/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). CARROLL, Steven, S. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). ELDRUP, Anne, B. [DK/US]; 2292 Faraday Avenue, Carlsbad, CA 92008 (US). MACCOSS, Malcolm [GB/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). OLSEN, David, B. [US/US]; 126 East Lincoln Avenue, Rahway, NJ
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— *without international search report and to be republished upon receipt of that report*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: NUCLEOSIDE DERIVATIVES AS INHIBITORS OF RNA-DEPENDENT RNA VIRAL POLYMERASE

(57) Abstract: The present invention provides nucleoside compounds and certain derivatives thereof which are inhibitors of RNA-dependent RNA viral polymerase. These compounds are inhibitors of RNA-dependent RNA viral replication and are useful for the treatment of RNA-dependent RNA viral infection. They are particularly useful as inhibitors of hepatitis C virus (HCV) NSSB polymerase, as inhibitors of HCV replication, and/or for the treatment of hepatitis C infection. The invention also describes pharmaceutical compositions containing such nucleoside compounds alone or in combination with other agents active against RNA-dependent RNA viral infection, in particular HCV infection. Also disclosed are methods of inhibiting RNA-dependent RNA polymerase, inhibiting RNA-dependent RNA viral replication, and/or treating RNA-dependent RNA viral infection with the nucleoside compounds of the present invention.

WO 2004/007512 A2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/21589

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C07H 19/14; A61K 31/70

US CL :536/27.2; 514/45

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/27.2; 514/45

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS structure search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Database CAPLUS on STN, AN 1993:160564. IIMORI et al. "A Study on Conformationally Restricted Sangivamycins and their Inhibitory Abilities of Protein Kinases". Nucleic Acids Symposium Series. 1992, Vol. 27, pages 169-170. Chemical Abstract, 1993. Vol. 118, Abstract No. 160564.	1-20
Y	MURAI et al. A Synthesis and an X-ray Analysis of 2'-C, 3'-C- and 5'-C-methylsangivamycins. Heterocycles. 1992, Vol. 33, Issue No. 1., pages 391-404. See entire document and attached Chemical Abstract, 1992, Vol. 116, Abstract No. 236073.	1-20

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

31 DECEMBER 2003

Date of mailing of the international search report

10 FEB 2004

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20531

Facsimile No. (703) 305-9230

Authorized officer

LAWRENCE ERIC CRANE

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/21589

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	IIMORI et al. 2'-C, 3'-C- and 5'-C-Methylsangivamycins: Conformational Lock with the Methyl Group. Tetrahedron Letters. 1991, Vol. 32, Issue No. 49, pages 7273-7276. See entire document and attached Chemical Abstract, 1992, Vol. 116, Abstract No. 106675.	1-3, 5-6
Y		1-20